DOCKET NO.: CELL-0086

Application No.: 09/450,999

Notice of Allowance Dated: December 11, 2003

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (canceled)

2. (previously presented) A compound according to Claim 16 in which R is a -CO₂H

group.

(previously presented) A compound according to Claim 16 in which Ra' is a 3.

hydrogen atom.

(previously presented) A compound according to Claim 16 in which Ra is a hydrogen 4.

atom or a hydroxyl group.

(previously presented) A compound according to Claim 16 in which (Alka), L1 is a -5.

CON(R²)- group.

(original) A compound according to Claim 5 in which (Alk^a)_rL¹ is a -CONH- group. 6.

(previously presented) A compound according to Claim 16 in which Ar² is a 1.4-7.

phenylene group optionally substituted with one or two atoms or groups -L²(Alk)_tL³(R⁴)₁₁.

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(original) A compound according to Claim 7 in which Ar² is a 1,4-phenylene group. 8.

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9. (previously presented) A compound according to Claim 16 in which Ar^1 is a pyrimidinyl, pyridyl or phenyl group optionally substituted with one or more atoms or groups $-L^2(Alk)_tL^3(R^4)_{tt}$.

- 10. (previously presented) A compound according to Claim 9 in which Ar^1 is a pyridyl or phenyl group optionally substituted with one or more atoms or groups $-L^2(Alk)_tL^3(R^4)_u$.
- 11. (original) A compound according to Claim 10 in which Ar¹ is a 3,5-dichloropyridin-4-yl group.
- 12. (previously presented) A compound according to Claim 16 in which R¹ is the group NHCOR³ or -NHR³.
- 13. (previously presented) A compound according to Claim 12 in which R^3 is a pyrrolidinyl or thiazolidinyl group optionally substituted with one or more halogen atoms, C_{1-6} alkyl groups, halo C_{1-6} alkyl groups optionally substituted with one or more hydroxyl groups, hydroxyl groups, C_{1-6} alkoxy groups, halo C_{1-6} alkoxy groups, thiol groups, C_{1-6} alkylthio groups, aromatic groups, heteroaromatic groups, or $-(Alk^2)_v R^{10}$ groups, and each nitrogen atom of the pyrrolidinyl or thiazolidinyl group is optionally substituted with a group $-(L^5)_p(Alk^3)_q R^{12}$;

or R^3 is a phenyl, pyrimidinyl or 1,3,5-triazinyl group optionally substituted with one or more atoms or groups $-R^{13a}$ or $-Alk^4(R^{13a})_m$.

14. (previously presented) A compound which is:

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3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-({4-[2-hydroxyethylamino]-6-methoxy-1,3,5-triazin-2-yl}amine)propanoic acid;

3-[(3,5-Dichloroisonicotinoyl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)-amino]phenyl}propanoic acid;

3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-[(2,6-dimethoxybenzoyl)amino]propanoic acid;

3-({[(4S)-3-Acetyl-1,3-thiazolinan-4-yl]carbonyl}amino-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid;

3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-[({(2S)-1-[(3,5-dichlorophenyl)sulphonyl]tetrahydro-1-H-pyrrol-2-yl}carbonyl)amino]propanoic acid;

 $(2RS,3RS)-3-\{4-[(3,5-\text{Dichloroisonicotinoyl})amino] phenyl\}-3-\{[((2S)-1-[(3,5-\text{dichlorophenyl})sulphonyl]tetrahydro-1-H-pyrrol-2-yl)carbonyl]amino\}-2-hydroxypropanoic acid;$

3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-[({2-[(2,5-dimethoxyphenyl)thio]-3-pyridinyl}carbonyl)amino]propanoic acid;

and the salts, hydrates and N-oxides thereof.

- 15. (previously presented) A pharmaceutical composition comprising a compound according to Claim 16 together with one or more pharmaceutically acceptable carriers, excipients or diluents.
- 16. (previously presented) A compound of formula (1):

$$Ar^{1}(Alk^{a})_{r}L^{1}Ar^{2}CH(R^{1})C(R^{a})(R^{a'})R \qquad (1)$$

wherein

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Ar¹ is an aromatic or C_{1-9} heteroaromatic group containing one to four heteroatoms seleted from oxygen, nitrogen, and sulfur, and is optionally substituted with one or more atoms or groups $-L^2(Alk)_tL^3(R^4)_u$;

 L^2 and L^3 , which may be the same or different, is each a covalent bond or a divalent linker atom or group selected from -O-, -S-, -C(O)-, -C(O)O-, -OC(O)-, -C(S)-, -S(O)-, -S(O)₂-, -N(R⁸)-, -CON(R⁸)-, -OC(O)N(R⁸)-, -CSN(R⁸)-, -N(R⁸)CO-, -N(R⁸)CO-, -N(R⁸)CO)₂-, -N(R⁸)CON(R⁸)-, -N(R⁸)CSN(R⁸)-, and -N(R⁸)SO₂N(R⁸)-;

 R^8 is a hydrogen atom or a C_{1-6} alkyl group optionally substituted with one or more halogen atoms, hydroxy groups, or C_{1-6} alkoxy groups;

t is zero or the integer 1;

u is an integer 1, 2 or 3;

Alk is an aliphatic or heteroaliphatic chain;

 R^4 is a hydrogen or halogen atom or a group selected from C_{1-6} alkyl, $-OR^5$, $-SR^5$, $-NR^5R^6$, $-NO_2$, -CN, $-CO_2R^5$, $-SO_3H$, $-SO_3R^5$, $-SOR^5$, $-SO_2R^5$, $-OCO_2R^5$, $-CONR^5R^6$, $-OCONR^5R^6$, $-CSNR^5R^6$, $-COR^5$, $-OCOR^5$, $-N(R^5)COR^6$, $-N(R^5)CSR^6$, $-SO_2N(R^5)(R^6)$, $-N(R^5)SO_2R^6$, $-N(R^5)CON(R^6)(R^7)$, $-N(R^5)CSN(R^6)(R^7)$, and $-N(R^5)SO_2N(R^6)(R^7)$; and

 R^5 , R^6 , and R^7 , which may be the same or different, is each a hydrogen atom or a straight or branched C_{1-6} alkyl group optionally substituted with one or more halogen atoms, hydroxy groups, or C_{1-6} alkoxy groups;

provided that when t is zero and each of L^2 and L^3 is a covalent bond, then u is the integer 1 and R^4 is other than a hydrogen atom;

 L^1 is a covalent bond or a linker atom or group selected from -CON(R²)-, -S(O)₂N(R²)-, -N(R²)-, and -O-;

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 R^2 is a hydrogen atom or a C_{1-3} alkyl group;

Ar² is a phenylene group optionally substituted with one or two atoms or groups $-L^2(Alk)_tL^3(R^4)_{11}$;

R¹ is a group selected from -NHCOR³, -NHSO₂R³, -NHR³, -NHC(O)OR³, $-NHCSR^3$, $-NHCON(R^3)(R^{3a})$, $-NHSO_2N(R^3)(R^{3a})$, and $-NHCSN(R^3)(R^{3a})$;

R³ is an optionally substituted C₃₋₁₀ cycloaliphatic group, an optionally substituted C₇₋₁₀ polycycloaliphatic group, an optionally substituted C₃₋₁₀ heterocycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, -S(O)₂-, -N(R⁸)-, $-C(O)NR^8$ -, $-OC(O)N(R^8)$ -, $-CSN(R^8)$ -, $-N(R^8)CO$ -, $-N(R^8)C(O)O$ -, $-N(R^8)CS$ -, - $S(O)_2N(R^8)$ -, $-N(R^8)S(O)_2$ -, $-N(R^8)CON(R^8)$ -, $-N(R^8)CSN(R^8)$ - and $-N(R^8)SO_2N(R^8)$ -; an optionally substituted C₇₋₁₀ heteropolycycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, -S(O)2-, $-N(R^8)$ -, $-C(O)NR^8$ -, $-OC(O)N(R^8)$ -, $-CSN(R^8)$ -, $-N(R^8)CO$ -, $-N(R^8)C(O)O_{-}, -N(R^8)CS_{-}, -S(O)_2N(R^8)_{-}, -N(R^8)S(O)_{2-}, -N(R^8)CON(R^8)_{-}, -N(R^8)CSN(R^8)_{-}$ and -N(R⁸)SO₂N(R⁸)-; an optionally substituted aromatic group, or an optionally substituted C₁₋₉ heteroaromatic group containing one, two, three or four heteroatoms seleted from oxygen, nitrogen, and sulfur;

R^{3a} is a hydrogen atom, an optionally substituted C₁₋₆ aliphatic group, an optionally substituted C₁₋₆ heteroaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, -S(O)2-, $-N(R^8)$ -, $-C(O)NR^8$ -, $-OC(O)N(R^8)$ -, $-CSN(R^8)$ -, $-N(R^8)CO$ -, $-N(R^8)C(O)O_{-}, -N(R^8)CS_{-}, -S(O)_2N(R^8)_{-}, -N(R^8)S(O)_{2-}, -N(R^8)CON(R^8)_{-}, -N(R^8)CSN(R^8)_{-}$ and -N(R⁸)SO₂N(R⁸)-, an optionally substituted C₃₋₁₀ cycloaliphatic group, an optionally Page 6 of 12

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substituted C₇₋₁₀ polycycloaliphatic group, an optionally substituted C₃₋₁₀ heterocycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, -S(O)₂-, -N(R⁸)-, $-C(O)NR^8-, -OC(O)N(R^8)-, -CSN(R^8)-, -N(R^8)CO-, -N(R^8)C(O)O-, -N(R^8)CS-, -S(O)_2N(R^8)-, -N(R^8)CO-, -N(R^8$, $-N(R^8)S(O)_2$ -, $-N(R^8)CON(R^8)$ -, $-N(R^8)CSN(R^8)$ - and $-N(R^8)SO_2N(R^8)$ -; an optionally substituted C₇₋₁₀ heteropolycycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, -S(O)₂-, $-N(R^8)$ -, $-C(O)NR^8$ -, $-OC(O)N(R^8)$ -, $-CSN(R^8)$ -, $-N(R^8)CO$ -, $-N(R^8)C(O)O_{-}, -N(R^8)CS_{-}, -S(O)_2N(R^8)_{-}, -N(R^8)S(O)_{2-}, -N(R^8)CON(R^8)_{-}, -N(R^8)CSN(R^8)_{-}$ and -N(R⁸)SO₂N(R⁸)-; an optionally substituted aromatic group, or an optionally substituted C₁₋₉ heteroaromatic group containing one, two, three or four heteroatoms seleted from oxygen, nitrogen, and sulfur;

wherein the optional substituents for the aromatic groups and the heteroaromatic groups of R³ and R^{3a} are selected from one or more atoms or groups R¹³ wherein R^{13} is $-R^{13a}$ or $-Alk^4(R^{13a})_m$;

R^{13a} is a halogen atom, or an amino, substituted amino, nitro, cyano, amidino, hydroxyl, substituted hydroxyl, formyl, carboxyl, esterified carboxyl, thiol, substituted thiol, $-COR^{14}$; $-CSR^{14}$, $-SO_3H$, $-SO_7^{14}$, $-SO_2R^{14}$, $-SO_2NH_2$, $-SO_2NHR^{14}$, $-SO_2N(R^{14})_2$, $-CONH_2$, $-CSNH_2$, $-CONHR^{14}$, $-CSNHR^{14}$, $-CON(R^{14})_2$, $-CSN(R^{14})_2$, $-N(R^{11})SO_2R^{14}$, $-N(SO_2R^{14})_2$, $-N(R^{11})SO_2NH_2$, $-N(R^{11})SO_2NHR^{14}$, $-N(R^{11})SO_2N(R^{14})_2$, $-N(R^{11})COR^{14}$, $-N(R^{11})CONH_2$, $-N(R^{11})CONHR^{14}$, $-N(R^{11})CON(R^{14})_2$, $-N(R^{11})CSNH_2$, $-N(R^{11})CSNHR^{14}$, $-N(R^{11})CSN(R^{14})_2$, -N(R¹¹)CSR¹⁴, -N(R¹¹)C(O)OR¹⁴, -SO₂NHet¹, -CONHet¹, -CSNHet¹, -N(R¹¹)SO₂NHet¹, -N(R¹¹)CONHet¹, -N(R¹¹)CSNHet¹, -SO₂N(R¹¹)Het², -Het², -CON(R¹¹)Het², -CSN(R¹¹)Het², -N(R¹¹)CON(R¹¹)Het², -N(R¹¹)CSN(R¹¹)Het², aryl or heteroaryl group;

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R¹⁴ is an -Alk⁴(R^{13a})_m, aryl or heteroaryl group;

NHet¹ is a C_{5-7} cyclicamino group optionally containing one or more -O- or -S- atoms or -N(R¹¹)-, -C(O)- or -C(S)- groups and optionally substituted with one or more substituents as defined for the cycloaliphatic groups of R³ and R^{3a};

Het² is a monocyclic C_{5-7} carbocyclic group optionally containing one or more -O- or -S- atoms or -N(R¹¹)-, -C(O) or -C(S)- groups and optionally substituted with one or more substituents as defined for the cycloaliphatic groups of R^3 and R^{3a} ;

Alk⁴ is a straight or branched $C_{1\text{-}6}$ alkylene, $C_{2\text{-}6}$ alkenylene or $C_{2\text{-}6}$ alkynylene chain, optionally interrupted by one, two, or three -O- or -S- atoms or -S(O)_n or -N(R¹⁵)-groups;

 R^{15} is a hydrogen atom or C_{1-6} alkyl group; m is zero or an integer 1, 2 or 3; n is an integer 1 or 2;

wherein the optional substituents for the aliphatic groups and the heteroaliphatic groups of R^{3a} are selected from halogen atoms, hydroxy groups, C_{1-6} alkoxy groups, thiol groups, C_{1-6} alkylthio groups, amino groups, and substituted amino groups;

wherein the optional substituents for the cycloaliphatic, polycycloaliphatic, heterocycloaliphatic and heteropolycycloaliphatic groups of R^3 and R^{3a} are selected from halogen atoms, C_{1-6} alkyl groups, halo C_{1-6} alkyl groups optionally substituted with hydroxyl groups, hydroxyl groups, C_{1-6} alkoxy groups, halo C_{1-6} alkoxy groups, thiol groups, C_{1-6} alkylthio groups, aromatic groups, heteroaromatic groups, and - $(Alk^2)_v R^{10}$ groups;

Alk² is a straight or branched C₁₋₃ alkylene chain; v is zero or an integer 1; DOCKET NO.: CELL-0086 PATENT

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 $R^{10} \text{ is a -OH, -SH, -N}(R^{11})_2, -CN, -CO_2R^{11}, -NO_2, -CON(R^{11})_2, -CSN(R^{11})_2, \\ -OC(O)N(R^{11})_2, -C(O)H, -COR^{11}, -OCO_2R^{11}, -OC(O)R^{11}, -C(S)R^{11}, -CSN(R^{11})_2, \\ -N(R^{11})COR^{11}, -N(R^{11})CSR^{11}, -SO_3H, -SOR^{11}, -SO_2R^{11}, -SO_3R^{11}, -SO_2N(R^{11})_2, -N(R^{11})SO_2R^{11}, -N(R^{11})CON(R^{11})_2, -N(R^{11})CSN(R^{11})_2, \text{ or -N}(R^{11})SO_2N(R^{11})_2 \text{ group; and}$

 R^{11} is an atom or group as defined for R^8 or an optionally substituted cycloaliphatic or hetercycloaliphatic group as defined for R^3 ;

and when R^3 is a heterocycloaliphatic group containing one or more nitrogen atoms each nitrogen atom is optionally substituted with a group $-(L^5)_p(Alk^3)_qR^{12}$;

$$L^5 \text{ is -C(O)-, -C(O)O-, -C(S)-, -S(O)-, -S(O)_2-, -CON(R^{11})-, -CSN(R^{11})-, -SON(R^{11})-, -SON(R^{11}$$

p is zero or an integer 1;

Alk³ is an optionally substituted aliphatic or heteroaliphatic chain; q is zero or an integer 1;

R¹² is a hydrogen atom or an optionally substituted cycloaliphatic, heterocycloaliphatic, polycycloaliphatic, polyheterocycloaliphatic, aromatic or heteroaromatic group;

 R^a and $R^{a'}$, which may be the same or different, are each independently selected from a hydrogen or halogen atom or an optionally substituted straight or branched alkyl, alkenyl, alkynyl, haloalkyl, alkoxy, haloalkoxy, alkylthio or - $(Alk^b)_m R^b$ group (in which Alk^b is a C_{1-3} alkylene chain, m is zero or the integer 1, and R^b is -OH, -SH, -NO₂, -CN, -CO₂H, -CO₂R^c (where R^c is an optionally substituted straight or branched C_{1-6} alkyl group), -SO₃H, -SOR^c, -SO₂R^c, -SO₃R^c, -OCO₂R^c, -C(O)H, -C(O)R^c, -OC(O)R^c, -C(S)R^c, -NR^dR^e (where R^d and R^e , which may be the same or different, are each a hydrogen atom or an optionally substituted straight or branched C_{1-6} alkyl group), -CON(R^d)(R^e),

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 $-OC(O)N(R^{d})(R^{e}), -N(R^{d})C(O)R^{e}, -CSN(R^{d})(R^{e}), -N(R^{d})C(S)R^{e}, -S(O)_{2}N(R^{d})(R^{e}),$

 $-N(R^d)SO_2R^e$, $-N(R^d)CON(R^e)(R^f)$ (where R^f is a hydrogen atom or an optionally substituted straight or branched C_{1-6} alkyl group), $-N(R^d)C(S)N(R^e)(R^f)$ or $-N(R^d)SO_2N(R^e)(R^f)$ group);

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Alk^a is an optionally substituted C_{1-6} aliphatic or C_{1-6} heteroaliphatic chain containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, -C(O)-, -C(S)-, -S(O)-, -S(O)-, $-N(R^8)$ -, -C(O)NR⁸-, -OC(O)N(R⁸)-, $-CSN(R^8)$ -, $-N(R^8)$ CO-, $-N(R^8)$ CO)-, $-N(R^8)$ CS-, -S(O)₂N(R⁸)-, $-N(R^8)$ CON(R⁸)-, $-N(R^8)$ CON(R⁸)-, and $-N(R^8)$ SO₂N(R⁸)-;

wherein the optional substituents for the aliphatic and heteroaliphatic groups of Alk^a are selected from halogen atoms, hydroxy groups, C_{1-6} alkoxy groups, thiol groups, C_{1-6} alkylthio groups, amino groups, and substituted amino groups;

r is zero or the integer 1;

R is a carboxylic acid (CO_2H), a carboxylic ester group, or carboxylic amide group; and the salts, hydrates and N-oxides thereof.

- 17. (previously presented) A method for the treatment of a mammal suffering from inflammatory arthritis, multiple sclerosis, allograft rejection, diabetes, inflammatory dermatoses, asthma or inflammatory bowel disease, comprising administering to the mammal a therapeutically effective amount of a compound according to Claim 16.
- 18. (canceled)

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19. (previously presented) A method according to Claim 17 wherein said inflammatory

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arthritis is selected from the group consisting of rheumatoid arthritis vasculitis and

polydermatomyositis.

20. (currently amended) A method according to Claim 19 Claim 17 wherein said

inflammatory dermatoses are selected from the group consisting of psoriasis and dermatitis.

21. (original) A method for inhibiting, in a mammal, the binding of $\alpha 4$ integrins to the

ligands thereof, comprising administering to the mammal an effective amount of a compound

according to Claim 16.

22. (original) A method according to Claim 21 wherein the α4 integrins are selected from

the group consisting of $\alpha 4\beta 1$ and $\alpha 4\beta 7$ integrins.